Urology Mythbusters: should hydronephrosis grade be used to decide which newborns should undergo voiding cystourethrogram?

Summary
In this episode of Mythbusters the premise that among infants with prenatally identified urinary tract dilation (UTD), voiding cystourethrogram (VCUG) should be performed in those with higher grade UTD but not in those with lower grade UTD is critically examined. It is concluded that severity of dilation is not strongly associated with risk of vesicoureteral reflux or other anomalies diagnosed by VCUG. Therefore, using hydronephrosis grade to decide which infants with UTD should undergo VCUG is not evidence based.

Urology Mythbusters’ mission: to rigorously evaluate the epithets, folklore, aphorisms and urban legends (or ‘urolegends’) that percolate through the field of urology.

Our goal: to go back to the original sources, evaluate the evidence, and determine the truth about each urolegend.

When we are done, each urolegend is given a final verdict:
De-bunked — nobody should be using this uro-myth for clinical care, except maybe Dr. Frankenstein, or Dr. Nick from the Simpsons.
Teeny, tiny nugget of truth — while there may be some validity underlying this uro-legend, there are too many unknowns to justify clinical application.
A big fat urologic maybe — evidence suggests that this might be true, but there are important areas of uncertainty.
I find your lack of faith disturbing — A valid clinical concept, with caveats.
True dat — Yup, this one actually seems to be based on solid evidence!

This edition’s urolegend
Among infants with prenatally identified urinary tract dilation (UTD), voiding cystourethrogram (VCUG) should be performed in those with higher grade UTD but not in those with lower grade UTD.

The context
The recommended postnatal evaluation for infants with prenatally diagnosed UTD remains controversial. While there is agreement that obtaining a postnatal ultrasound to reassess the anatomy is appropriate, recommendations regarding indications for VCUG are less clear. Although VCUG has historically been considered a standard part of the UTD postnatal evaluation, this test is increasingly seen as invasive and noxious, with exposure to radiation and iatrogenic adverse effects such as UTI. Furthermore, evidence-based reviewers have questioned the value of diagnosing vesicoureteral reflux (VUR) [1]. These trends have coincided with efforts to restrict VCUG utilization to more specific subpopulations, exemplified by the American Academy of Pediatrics (AAP) guidelines on management of infants after initial febrile UTI, which recommended deferring VCUG until after a second UTI [2].

Current guidelines generally indicate that the degree of UTD should be the basis for decision-making regarding VCUG. However, it is unclear that there is an evidence-based rationale for restricting VCUG to infants with higher grade UTD or whether the decision to perform a VCUG in infants with UTD should be independent of the degree of dilation.

The origin
Since early in the prenatal screening era, it has been recognized that multiple urological anomalies are often present in the same patient. Figures as high as 50% have been quoted for the proportion of infants with ureteropelvic junction obstruction (UPJO) who have associated urologic anomalies [3]; these numbers have driven recommendations for additional testing in such patients. The 1998 edition of Campbell’s Urology stated that ‘it is imperative...
to obtain a voiding cystourethrogram in every patient with ureteropelvic junction obstruction’ to identify VUR [3]. Guideline panels continue to recommend VCUG for selected infants with UTD. The American Urological Association (AUA) guidelines for primary VUR in children, published in 2010 and updated in 2017, make recommendations for screening for VUR (via VCUG) in infants with UTD. These guidelines state that VCUG ‘is recommended for children with high-grade (Society of Fetal Urology [SFU] grade 3 and 4) hydronephrosis’ and that for children with SFU grade 1 or 2, it is ‘considered an option to perform a voiding cystourethrogram in these patients to screen for VUR.’ [4] Similarly, the report of the multidisciplinary consensus panel that developed the ‘UTD’ grading system recommended that infants with high risk (UTD P3) on postnatal imaging should undergo VCUG, while evaluation with VCUG in infants with UTD P1 and P2 is ‘left to the discretion of the clinician.’ [5] The SFU consensus statement on postnatal evaluation of antenatal hydronephrosis also recommends that postnatal VCUG be performed in infants with moderate-to-severe postnatal UTD, with VCUG in cases of mild UTD at the discretion of the clinician [6]. Recommendations from the European Society for Pediatric Radiology also indicate VCUG for those with higher grades of UTD, but not for SFU II or lower [7].

The evidence

With respect to the prevalence of VUR among infants with UTD, multiple reviews and meta-analyses have been performed to estimate how common concurrent VUR is in this population. There is general consensus that VUR prevalence is higher among infants with UTD than in the general population. A meta-analysis by Lee et al. found that among 1308 subjects with varying degrees of prenatal UTD, the overall risk of VUR was 8.6%, which they described as ‘quantifiably higher than the general population incidence (1%)’ [8]. Another meta-analysis by Weitz and Schmidt [9] found strikingly similar results, with an overall prevalence of VUR of 8.2% in the UTD population.

Other individual center series have reported significantly higher VUR prevalence in infants with UTD. For example, in a large prospective series, Braga et al. analyzed 334 patients with prenatally diagnosed UTD, and among the 238 who underwent VCUG, VUR was present in 23.9% [10] (Even if it is assumed that 0% VUR among the 96 patients who did not undergo VCUG, this would still result in overall VUR prevalence of 17%). Similarly, Estrada et al. reported on 1514 patients with SFU grade II dilation, and among the 1150 (76%) who underwent VCUG, VUR was present in 28% [11].

However, there is also substantial evidence that VUR is not significantly more common in infants with higher grade UTD. For example, the meta-analysis by Lee et al. found that the risk of VUR was similar for all degrees of antenatal hydronephrosis [8]. Most other individual series have reported similar results: Hwang et al. actually observed that VUR prevalence was highest in the mild UTD group: 31.4% (34/108) in the mild UTD group vs 7.9% (7/89) in the moderate UTD group vs 15.2% (12/79) in the severe UTD group (chi-squared P-value calculated at <0.0001, although not reported in the article) [12]. Coelho et al. observed VUR in 10.1% of mild UTD (9/89), 8.3% of moderate UTD (5/60), and 4.7% of severe UTD (2/43) (chi-squared P-value calculated at 0.568, although not reported in the article) [13]. Zareba et al. observed VUR in 25.8% of high-grade (SFU 3–4) UTD (33/128) vs 18.5% of low-grade (SFU 1–2) UTD (46/248) (chi-square P-value calculated at 0.1028, although not reported in the article) [14].

One series that appears to contradict these findings was the small series from Grazioi et al. [15] They reported the postnatal findings on 89 patients with prenatally identified UTD and found that overall VUR prevalence was 2.8% (1/36) among mild UTD, 12.5% (3/24) among moderate UTD, and 20.7% (6/29) among severe UTD (chi-square P-value calculated at 0.0736, although not reported in the article). However, it should be noted that in this series, the ‘mild’ group included patients with anteroposterior (AP) diameter (APD) of 0–6 mm, which would be considered ‘normal’ by most standards. Thus, the apparent trend toward increased prevalence of VUR among more severe UTD patients may have been influenced by inclusion of these normal patients. If only the ‘moderate’ (7–9 mm APD) and the ‘severe’ groups (≥10 mm APD) are included, the difference between UTD groups in VUR risk will be non-significant (P-value = 0.429).

One might argue that although overall VUR prevalence does not vary by UTD grade, risk of severe VUR is higher among those with higher grade UTD, and so this justifies VCUG screening. The data regarding this are more limited. The meta-analyses by Lee et al. and Weitz and Schmidt did not stratify by VUR grade [8,9], and Coelho et al. did not report VUR grade as a function of UTD grade [13].

Hwang et al. reported rates of high-grade (≥III) VUR and still did not observe higher risk in the severe UTD group: High-grade VUR was seen in 21 of 108 renal units (19.4%) with mild UTD vs 6 of 89 renal units (6.7%) with moderate UTD vs 11 of 79 (13.9%) with severe UTD (chi-square P-value calculated at 0.036, although not reported in the article) [12]. Similar findings were observed in a small series by Kangin et al. who reported VUR grades among infants with antenatal UTD. They did not present overall VUR prevalence stratified by UTD grade but instead reported only on those patients who had any VUR. Among 56 renal units with any VUR, the proportion that had high-grade (≥III) VUR was similar regardless of UTD severity (96% [24/25 renal units with mild UTD vs 77.3% [17/22] of renal units with moderate UTD vs 77.8% [7/9] of renal units with severe UTD) (chi-square P-value calculated at 0.142, although reported only as >0.05 in the article).

A multicenter series from Herndon et al. reported findings in infants with prenatual UTD who were confirmed postnatally to have VUR [16]. Thus, overall VUR risk could not be assessed, and authors did not specifically report VUR grade stratified by UTD severity. However, it is notable that among the 71 patients and 116 renal units with VUR, 88% (102 renal units) had AP diameter <10 mm. Despite this, 74 renal units had VUR grade >III, indicating clearly that a large number of ‘mild’ UTD cases had high-grade VUR.

Some groups have noted higher risk of severe VUR in the higher severity UTD group. In the small series from Grazioi et al. all five patients with VUR > grade II were in the ‘severe’ UTD group (5/29), and there were no higher grade VUR cases among the 60 patients with AP diameter < 10 mm [15]. Similarly, Zareba et al. observed high-grade VUR in just 0.4% (1/248) in SFU 1–2 UTD vs 14.1% (18/128) in SFU 3–4 UTD (chi-square P-value calculated at <0.0001,
Although severity of renal dilation alone does not correlate well with VUR risk, ureteral dilation may be a better predictor. The data are surprisingly limited regarding the significance of ureteral dilation on subsequent VCUG findings or postnatal UTI risk. There is some evidence that patients with ureteral dilation are at independently higher risk of VUR as well as postnatal UTI [14,17], although many of the patients in these series had non-refluxing megaureters, and one large series found that ureteral dilation was not associated with UTI [18]. Data from a large cohort of children undergoing imaging after UTI found that ureteral dilation on ultrasound was significantly associated with VUR and that the association was much stronger for high-grade VUR [19]. It is not clear if this association holds strongly for infants with prenatal UTD, who were excluded from this analysis.

Overall, therefore, there is little evidence that VUR (high-grade or otherwise) is significantly more common among infants with more severe UTD. Of course, VUR is not the only condition diagnosed on VCUG. One might argue that the need to rule out lower urinary tract obstruction (LUTO) is even more important than diagnosing VUR. Clearly, it is of critical importance that posterior urethral valves (PUVs) or other causes of obstruction not be missed, and one might argue that the recommendation to perform VCUG in infants with severe UTD ensures this. The question, however, is whether higher grades of UTU alone should trigger concern about LUTO in the absence of other specific findings. In fact, it is very rare for PUV to present with isolated renal UTU as the only abnormality. Almost all infants with LUTO are identified based on bladder enlargement and wall thickening, hydronephrosis, echogenic kidneys, a history of oligohydramnios, or a combination of these [20–22]. For example, Chitrit et al. compared ultrasound findings among infant boys with confirmed LUTO to boys with VUR but without LUTO [23] and observed substantial differences in bladder size, bladder wall thickening, posterior urethral dilation, and other findings. The conclusion is that it would be vanishingly rare for LUTO to present with isolated hydrenephrosis (even high grade) without any lower tract abnormality or ureteral dilation (or oligohydramnios prenatally). Deferring VCUG in patients with UTU but without such additional findings is extremely unlikely to result in missed cases of PUV.

One might also hypothesize that in cases of suspected UPJO, one needs to rule out VUR as the cause of the UPJO. Although this phenomenon has been documented, it is quite uncommon. In one series of 147 patients undergoing pyeloplasty for UPJO, just 14% had concurrent VUR [24], and in only 3.3% was obstruction secondary to the VUR itself. In these cases, the treatment was pyeloplasty, just as in the cases where VUR was incidental. Bomalaski et al. also reviewed their experience with 41 patients with both UPJO and VUR [25] and did not observe convincing evidence of VUR as a cause of obstruction. In fact, of the patients with both VUR and UPJO who underwent reimplantation as initial treatment, all subsequently required pyeloplasty, suggesting that correction of VUR in these patients did not result in resolution of obstruction. These limited data suggest that patients with obstruction caused by VUR are very rare, and even in such rare cases, the initial treatment is the same as that for primary UPJO (pyeloplasty). Thus, VCUG in all patients with suspected UPJO may not be warranted based on concerns for VUR as the cause of obstruction.

Finally, we have heard statements by respected authorities that VUR is more dangerous when associated with concurrent obstructive UTU (compared to isolated VUR without obstruction), due to greater risk of ‘seeding’ of the obstructed system with microorganisms and resulting severe infection. It has long been recognized that the combination of infection and obstruction can lead to serious illness, and there have been reports of patients whose obstruction transiently worsened in the setting of severe infection [26]. However, we are not aware of any direct evidence that the mere presence of VUR is associated with more frequent or worse infection in patients with obstructive UTU; this would be a fruitful area for further research.

The closing statement

The literature demonstrates that there is no strong association between severity of UTU and subsequent findings on VCUG, particularly VUR. Neither overall VUR nor high-grade VUR is significantly more common among infants with more severe upper tract dilation in most series. Thus, it is irrational to perform VCUG in infants with more severe UTU based on the premise that the VCUG will have a significantly higher yield in such infants. If one believes that identification of VUR is essential in all infants, then all infants with postnatally confirmed UTU should undergo VCUG because VUR appears to be more common among infants with UTU than infants without UTU, even though prevalence is similar across UTU grades. Alternatively, one might choose to selectively screen based not on degree of dilation but on the presence of additional ultrasound findings (e.g. bladder enlargement and/or thickening) that are associated with more severe anomalies such as LUTO.

The verdict: Teeny, tiny nugget of truth

The evidence shows that hydronephrosis grade alone (whether measured by SFU, UTU, APD, or other scores) is not strongly associated with risk of VUR or other anomalies diagnosed by VCUG (although the presence of UTU of any grade increases the likelihood that VUR is also present). Therefore, using hydronephrosis grade to decide which infants with UTU should undergo VCUG is not evidence based, and the decision to proceed with VCUG should not be based simply on the degree of UTU. Rather, VCUG should be performed based on the presence of specific findings that substantially increase the likelihood of high-grade VUR and/or UTI, such as ureteral dilation, or findings highly associated with LUTO, including megacystis, bladder wall thickening, and/or severe bilateral UTU in a male.

Author statements

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Competing interests

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References


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